

Delayed Childbearing and Risk of Adverse Perinatal Outcome

A Population-Based Study

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Objective.—To investigate the effect of advancing maternal age on pregnancy outcome among healthy nulliparous women, after adjustment for demographic characteristics, smoking, history of infertility, and other medical conditions.

Design.—A population-based cohort study was conducted with prospectively collected data from the Swedish Medical Birth Register.

Patients.—Nulliparous Nordic women (N=173 715), aged 20 years and above, who delivered single births at Swedish hospitals from 1983 through 1987.

Outcome Measures.—Late fetal and early neonatal death rates; rates of very low birth weight (VLBW, <1500 g), moderately low birth weight (MLBW, 1500 through 2499 g), very preterm delivery (≤ 32 weeks), moderately preterm delivery (33 through 36 weeks), and small-for-gestational-age (SGA) infants (< -2 SDs).

Results.—Compared with women aged 20 to 24 years, women aged 30 to 34 years had significantly higher adjusted odds ratios (ORs) of late fetal deaths (OR=1.4); VLBW (OR=1.2); MLBW (OR=1.4); very preterm birth (OR=1.2); and SGA infants (OR=1.4). Among women aged 35 to 39 years, the adjusted OR was significantly higher for VLBW (OR=1.9); MLBW (OR=1.7); very preterm birth (OR=1.7); moderately preterm birth (OR=1.2); and SGA infants (OR=1.7). Among women 40 years old and older, the adjusted OR was significantly higher for VLBW (OR=1.8); MLBW (OR=2.0); very preterm birth (OR=1.9); moderately preterm birth (OR=1.5); and SGA infants (OR=1.4).

Conclusions.—Delayed childbearing is associated with an increased risk of poor pregnancy outcomes after adjustment for maternal complications and other risk factors.

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INCREASING maternal age and nulliparity are associated with an increased risk of poor pregnancy outcomes.¹⁻⁴ Al-

though the reported increases in risk are modest,² the impact of delayed childbearing becomes more important as the phenomenon becomes more prevalent.

In the United States, the rates of first births to women aged 30 years and above have increased dramatically during the last decades. From 1975 through 1986, the rates increased from 8.0 to 17.5 per 1000 women aged 30 to 34 years, from 1.9 to 4.7 per 1000 among women aged 35 to 39 years, and from 0.3 to 0.6 among women aged 40 to 44 years.⁵ This increase in the rate of delayed childbear-

ing is attributed to women voluntarily postponing pregnancies for personal, educational, or professional reasons.⁶ The number of children born to nulliparous women aged 30 years and above increased from 1975 through 1986 from 69 000 to 230 000.⁵ A portion of the increase in the number of births to nulliparous women aged 30 years and above is owing to the large birth cohorts following the Second World War. As this "baby boom" continued up to the mid-1960s, the absolute number of deliveries among women over the age of 30 years is expected to continue to increase.⁷

In examining the public health effects of delayed childbearing, conclusions based on results from population-based studies can be generalized, whereas findings from any other sampling frame are limited to the specific study population. Studies should also have sample sizes of sufficient power to detect differences in outcomes, such as late fetal death, after adjustment for confounding factors. The factors that potentially confound the maternal age-pregnancy outcome relationship can be extensive. For example, a history of previous infertility or certain pregnancy complications are more prevalent among older women and are related to the risk of adverse pregnancy outcomes.^{2,8} Since the intent is to address the risks of increasing age among women with uncomplicated pregnancies, the effect of these factors needs to be separated from that of age alone on poor pregnancy outcomes. While a few earlier studies were population-based with sufficient power to detect age effects on rare outcomes, information about confounding factors has been limited^{1,3,4} and

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collected retrospectively.^{3,4}

In Sweden, delayed childbearing is more common than in the United States and, for the same reasons as in the United States, has increased through the last decade. As an example, from 1980 through 1990, the rate of first births increased from 15.6 to 28.7 per 1000 women aged 30 to 34 years.⁹ The Swedish Medical Birth Register, a population-based birth register with prospectively collected data on maternal age, other sociodemographic characteristics, previous infertility problems, and medical complications during pregnancy, provided a unique opportunity to examine the effect of advancing maternal age on pregnancy outcome among nulliparous women before and after adjustment for known confounding factors.

METHODS

From 1983 through 1987, a total of 487 000 births were recorded on the Swedish Medical Birth Register. For the purposes of this study, the population consisted of single births to all nulliparous women of Nordic citizenship, aged 20 years and above (N=173 715).

The Swedish Medical Birth Register receives the following information on all hospital births: demographic data; maternal reproductive history; and complications during pregnancy, delivery, and the neonatal period. This information is prospectively collected from the first antenatal visit. The Medical Birth Register includes more than 99% of all births in Sweden.¹⁰ All births and deaths are validated by comparison with similar data reported to a parish-based population register. The mother's unique personal identification number links the birth and the parish-based registers.¹¹ Similarly, this identification number was used to link the birth register to a population-based register by Statistics, Sweden, to obtain information on maternal education.¹²

DATA ANALYSIS

Multiple logistic regression analyses were computed to estimate the effect of maternal age on the risk of late fetal death, early neonatal death, low birth weight, preterm delivery, and small-for-gestational-age (SGA) infants.¹³ Odds ratios (ORs) were calculated to approximate the relative risk, with women aged 20 to 24 years as the reference group. The ORs were estimated before and after adjustment for confounding factors, using PROC LOGIST in the SAS software program package.^{14,15}

Among the dependent variables in the analysis, late fetal death was defined as a stillbirth occurring at a gestation of 28 weeks or longer. Early neonatal death

was defined as a death occurring during the first 6 completed days of life. Low birth weight was divided into very low birth weight (VLBW, <1500 g) and moderately low birth weight (MLBW, 1500 through 2499 g). Preterm delivery was divided into very preterm delivery (≤ 32 completed weeks) and moderately preterm delivery (33 through 36 completed weeks).

The SGA infants were defined as having birth weights that were less than 2 SDs below the mean birth weight for gestational age according to the Swedish birth-weight curve.¹⁶ Gestational age was assessed by ultrasonic measurements in 29% or estimated from the date of the last menstrual period in 71%. Midwives are generally instructed to use ultrasound to estimate gestational age if menstrual periods are irregular or the last bleeding is a withdrawal bleeding from oral contraceptives. In Sweden, more than 95% of the pregnant women attend antenatal care before the 15th gestational week.¹⁷

The following independent variables were treated categorically in the analysis: maternal age, years of formal education, cohabitation with the infant's father, maternal smoking habits, history of infertility, and maternal diseases or complications during pregnancy. Maternal age was defined as age in years at the infant's birth and stratified into 5-year age groups for all analyses, except for the analysis of late fetal and early neonatal deaths, in which the small numbers of deaths among women aged 40 years and older were combined with deaths among women aged 35 to 39 years. Maternal education was based on years of formal education and categorized into five levels corresponding to the Swedish school system. Information about cohabitation with the father, smoking habits, and previous infertility problems was collected by midwives at the woman's first antenatal visit. Previous infertility problems were expressed as the number of years of involuntary childlessness. Between 4% and 7% of the data on education, cohabitation with the infant's father, or smoking were missing owing to incomplete data entry.

Complications during pregnancy and delivery were classified according to the *International Classification of Diseases, Eighth Revision (ICD-8)* through 1986 and thereafter the *Ninth Revision (ICD-9)*. They were divided into three groups for the purpose of this analysis: hypertensive diseases, defined as essential hypertension and pregnancy-induced hypertension (ICD-8 codes 401 and 637 and ICD-9 code 642); diabetes mellitus, defined as insulin-dependent

diabetes and gestational diabetes (ICD-8 code 250 and ICD-9 codes 250, 648.0, and 648.8); and antepartum hemorrhage, defined as delivery complicated by abruptio placentae, placenta previa, or other antepartum hemorrhage (ICD-8 code 651 and ICD-9 code 641).

RESULTS

Late Fetal and Early Neonatal Deaths

The rates of late fetal death increased with increasing maternal age (Table 1). The rates of early neonatal death were higher among women aged 35 years and older compared with women aged 20 to 34 years. All of the independent variables were associated with late fetal and early neonatal deaths. Maternal education showed a weak U-shaped relationship. Women who cohabited with the infant's father and nonsmokers had the lowest rates of late fetal and early neonatal deaths. Compared with women who had been infertile for less than 3 years, women who had been infertile for at least 3 years had higher rates of late fetal and early neonatal deaths. Women with any of the three groups of pregnancy complications had higher rates of late fetal and early neonatal deaths than women without complications. The low incidence of diabetes (0.7%) suggests underreporting. Women with antepartum hemorrhage had the highest rates of late fetal and early neonatal deaths of all women.

These independent variables also influenced the rates of low birth weight, preterm delivery, and SGA infants (data not shown). Importantly, these independent variables also were associated with the major independent variable, maternal age (Table 2). More younger mothers than older mothers had no more than 9 years of education or were daily smokers. On the other hand, not cohabiting with the infant's father, infertility for at least 1 year, and diagnoses of hypertensive diseases, diabetes, and antepartum hemorrhage were more common among older mothers than younger mothers. We therefore adjusted the estimates for the effects of other variables using multiple regression analyses (Tables 3 through 5).

Compared with women aged 20 to 24 years, the crude ORs for late fetal death increased with maternal age from 30 to 34 years to 35 years and above (Table 3). After adjustment for confounding factors, the ORs for late fetal death were statistically significant for women aged 30 to 34 years (1.4) and just missed significance for women aged 35 years and above (1.4). The adjusted ORs for early neonatal deaths were not statistically significantly higher among women aged 30 years and above.

Table 1.—Number of Single Births and Deaths to Nordic Nulliparous Women, by Maternal Sociodemographic Characteristics and Pregnancy Complications

	No. of Births	Late Fetal Death		Early Neonatal Death	
		No.	Rate/1000 Births	No.	Rate/1000 Live Births
Maternal age, y					
20-24	70 557	251	3.6	212	3.0
25-29	68 846	253	3.7	177	2.6
30-34	26 241	125	4.8	78	3.0
35-39	6811	34	5.0	33	4.9
40-52	1069	7	6.5	5	4.7
Missing	191	2	...	0	...
Education, y					
≤9	31 774	122	3.8	110	3.5
10-11	72 745	299	4.1	204	2.8
12	17 079	54	3.2	33	1.9
13-14	26 696	80	3.0	62	2.3
≥15	17 705	69	3.9	67	3.8
Missing	7716	48	6.2	29	3.8
Cohabiting with infant's father					
Yes	155 146	568	3.7	420	2.7
No	11 967	60	5.0	34	2.9
Missing	6602	44	6.7	51	7.8
Cigarette smoking					
No	113 267	395	3.5	293	2.6
1-9/d	31 036	136	4.4	99	3.2
>9/d	17 948	88	4.9	45	2.5
Missing	11 464	53	4.6	68	6.0
Infertility, y					
0	155 998	596	3.8	447	2.9
1-2	10 124	38	3.8	30	3.0
≥3	7593	38	5.0	28	3.7
Hypertensive diseases					
No	160 700	611	3.8	453	2.8
Yes	13 015	61	4.7	52	4.0
Diabetes					
No	172 587	660	3.8	498	2.9
Yes	1128	12	10.6	7	6.3
Antepartum hemorrhage					
No	171 505	584	3.4	455	2.7
Yes	2210	88	39.8	50	23.6
Total	173 715	672	3.9	505	2.9

Table 2.—Distribution of Sociodemographic Characteristics and Pregnancy Complications According to Maternal Age*

	Maternal Age, y, %			
	20-24	25-29	30-34	≥35
Education, ≤9 y	26	13	12	15
Not cohabiting with infant's father	8	5	7	13
Daily smoker	34	24	24	24
Infertility, ≥1 y	4	11	18	28
Hypertensive diseases	7	7	8	10
Diabetes	0.6	0.5	0.8	1.2
Antepartum hemorrhage	1.1	1.2	1.6	1.9

*N=173 715.

Low Birth Weight

The overall rates of VLBW and MLBW were 0.6% and 4.0%, respectively. Compared with women aged 20 to 24 years, the crude ORs of VLBW and MLBW were higher among

women aged 30 years and above (Table 4). Both the crude and adjusted ORs of VLBW and MLBW increased with maternal age, except for the adjusted ORs of VLBW, which were similar for the 35-through-39-year and 40-year-and-above age groups (1.9 and 1.8, respec-

tively). Among women aged 35 years and above, the adjusted ORs of VLBW were lower than the crude ORs because of the substantial effect of age-related diseases like antepartum hemorrhage and hypertensive diseases.

Preterm Delivery

The overall rates of very preterm and moderately preterm deliveries were 1.1% and 5.4%, respectively. Compared with women aged 20 to 24 years, the adjusted ORs of very preterm deliveries were higher among women aged 30 years and above and increased with maternal age (30 to 34 years, 1.2; 35 to 39 years, 1.7; 40 years and above, 1.9). The adjusted ORs of moderately preterm deliveries were higher among women aged 35 years and above and increased with maternal age (Table 5).

SGA Infants

The overall rate of SGA births was 2.8%. Compared with women aged 20 to 24 years, the crude ORs of SGA infants were higher among women aged 30 years and above and increased with maternal age from 30 to 34 years (1.2) to 35 to 39 years (1.5), but declined thereafter (1.3) (Table 6). The ORs were higher after adjustment because smoking, the major risk factor for SGA infants, was more prevalent in the reference group than among delayed childbearers (Table 2).

COMMENT

This study demonstrates that delayed childbearing among nulliparous women with uncomplicated pregnancies is associated with increased risks of poor pregnancy outcomes. Specifically, women aged 30 years and above faced a 40% increased risk of late fetal death compared with women aged 20 to 24 years after adjustment for several major confounding factors. Among women aged 35 years and above the risk of low birth weight, preterm delivery, and SGA infants generally increased with maternal age from 20% to twofold. These results were in agreement with previous investigations with the power to detect statistically significant differences in death rates.^{1,3,4,18}

A strength of the present study lies in the ability to adjust for possible confounding factors and thus separate the influence of maternal age and medical or socioeconomic factors associated with age. In general, maternal diseases, pregnancy complications, and a previous history of infertility are considered the main potential confounding factors.^{2,18} In the

Table 3.—Crude and Adjusted Odds Ratios for Late Fetal and Early Neonatal Death by Maternal Age

Maternal age, y	Late Fetal Death (n=173 524)		Early Neonatal Death (n=172 854)	
	Crude Odds Ratio	Adjusted* Odds Ratio (95% Confidence Interval)	Crude Odds Ratio	Adjusted* Odds Ratio (95% Confidence Interval)
20-24	1.0	1.0	1.0	1.0
25-29	1.0	1.1 (0.9-1.3)	0.9	0.9 (0.7-1.1)
30-34	1.3	1.4 (1.1-1.8)	1.0	0.9 (0.7-1.2)
≥35	1.5	1.4 (0.995-2.0)	1.6	1.3 (0.9-2.0)

*Adjustments were made for maternal education, cohabiting with infant's father, maternal smoking, infertility, hypertensive diseases, diabetes, and antepartum hemorrhage.

Table 4.—Crude and Adjusted Odds Ratios for Very Low Birth Weight (<1500 g) and Moderately Low Birth Weight (1500 Through 2499 g) by Maternal Age*

Maternal age, y	<1500 g		1500-2499 g	
	Crude Odds Ratio	Adjusted† Odds Ratio (95% Confidence Interval)	Crude Odds Ratio	Adjusted† Odds Ratio (95% Confidence Interval)
20-24	1.0	1.0	1.0	1.0
25-29	0.9	1.0 (0.9-1.1)	1.0	1.1 (1.01-1.1)
30-34	1.2	1.2 (1.03-1.5)	1.2	1.4 (1.3-1.5)
35-39	2.2	1.9 (1.5-2.4)	1.6	1.7 (1.5-1.9)
≥40	2.5	1.8 (1.04-3.0)	2.0	2.0 (1.5-2.5)

*n=171 619.

†Adjustments were made for maternal education, cohabiting with infant's father, maternal smoking, infertility, hypertensive diseases, diabetes, and antepartum hemorrhage.

Table 5.—Crude and Adjusted Odds Ratios for Very Preterm Delivery (≤32 wk) and Moderately Preterm Delivery (33 Through 36 wk) by Maternal Age*

Maternal age, y	≤32 wk		33-36 wk	
	Crude Odds Ratio	Adjusted† Odds Ratio (95% Confidence Interval)	Crude Odds Ratio	Adjusted† Odds Ratio (95% Confidence Interval)
20-24	1.0	1.0	1.0	1.0
25-29	0.9	1.0 (0.9-1.1)	1.0	1.0 (0.9-1.0)
30-34	1.1	1.2 (1.04-1.4)	1.0	1.0 (0.97-1.1)
35-39	1.7	1.7 (1.4-2.1)	1.2	1.2 (1.1-1.3)
≥40	2.2	1.9 (1.2-2.9)	1.6	1.5 (1.2-1.8)

*n=172 230.

†Adjustments were made for maternal education, cohabiting with infant's father, maternal smoking, infertility, hypertensive diseases, diabetes, and antepartum hemorrhage.

present study, the influence of maternal age on late fetal death, low birth weight, preterm delivery, and SGA infants persisted after adjustment for hypertension, diabetes, and antepartum hemorrhage. The age-related increased ORs of late fetal death and SGA infants may indicate a progressive decrease in uteroplacental perfusion with advancing maternal age. The previously reported advancing myometrial atherosclerosis with age among women under 40 years of age supports this hypothesis.¹⁹

Previous spontaneous abortions and subfecundity have been associated with maternal age.²⁰⁻²² In the present study, women with previous infertility problems included those with difficulties in conceiving and/or with spontaneous

abortions. Similar to earlier studies,¹ this variable was not statistically significantly associated with the risk of late fetal or early neonatal death in the multiple regression analysis.

Sociodemographic factors and access to antenatal and obstetrical care may be unevenly distributed among women of different ages and perinatal outcomes.^{23,24} In general, nulliparous women aged 30 years and above are better educated, smoke less, and attend antenatal care earlier than younger nulliparous women.²⁴ Thus, without adjustment for these variables, the observed age-related risks of perinatal mortality may be underestimated. In this study, adjustments were made for maternal educational level, smoking habits, and cohab-

Table 6.—Crude and Adjusted Odds Ratio for Small-for-Gestational-Age Infants (<-2 SDs) by Maternal Age*

Maternal age, y	Crude Odds Ratio	Adjusted† Odds Ratio (95% Confidence Interval)
20-24	1.0	1.0
25-29	1.0	1.1 (1.04-1.2)
30-34	1.2	1.4 (1.3-1.6)
35-39	1.5	1.7 (1.5-2.0)
≥40	1.3	1.4 (1.01-2.0)

*n=171 005.

†Adjustments were made for maternal education, cohabiting with infant's father, maternal smoking, infertility, hypertensive diseases, diabetes, and antepartum hemorrhage.

iting with the infant's father without dramatic effects on the ORs of poor pregnancy outcomes. Moreover, since antenatal care and obstetrical care are free in Sweden and more than 95% of pregnant women attend antenatal care before the 15th gestational week, access to care probably did not influence the results of the present study.¹⁷

Information on other potential confounding factors, such as maternal nutrition and infections during pregnancy, was not available.^{25,26} These factors may be associated with socioeconomic status and maternal smoking,²⁷ which were controlled in the present analyses.

In general, these results agree with previous investigations.^{1-4,18} However, during recent years, the results of several hospital-based studies did not demonstrate increased risks of adverse perinatal outcomes with increasing maternal age.^{20,28,29} One of these studies had insufficient power to detect an increase in the relative risk of low birth weight.²⁰ In the second study, the study population was also small, but the number of low-birth-weight infants was not reported, and it was therefore impossible to make power calculations.²⁸ The data for the third study were derived from the private service of a single hospital, and the age distribution among nulliparous women of this population was very different from the usual pattern, suggesting that the findings from this study are only characteristic of the specific private hospital population studied.²⁹

In the US population, there is extensive ethnic and socioeconomic diversity compared with the relatively homogeneous Swedish population. However, the US subpopulation of delayed child-bearers is dominated by white middle-class and upper-middle-class women who, like their Swedish counterparts, receive antenatal care early.^{6,8} Like Sweden, there is a continual increase over time in the rates of first births among

women aged 30 years and above. We are unaware of any population-based US data set that includes information on sociodemographic variables, history of infertility, and medical complications during pregnancy and delivery. The use of the Swedish data were therefore the

obvious choice. Thus, the present results have ramifications for the United States.

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